Our Reference No. 9579-37

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Gary Levy**

Serial No. **09/902,563**

Filed: **July 12, 2001**

For: **Methods of Modulating Immune Coagulation**

Group No.: 1644

Examiner: Maher M. Haddad

DECLARATION UNDER 37 C.F.R. 1.132

Honourable Assistant Commissioner
For Patents
Washington, D.C. 20231

Dear Sir:

I, Gary Levy, citizen of Canada and resident of Toronto, Ontario, Canada declare that the following facts are within my knowledge and are true.

1. I am the named inventor of the above-referenced patent application (hereinafter "the application").

2. I am the Director of the Multi-Organ Transplant Program at the Toronto General Hospital and a Professor of Medicine at the University of Toronto, Toronto, Ontario, Canada. I attach a copy of my curriculum vitae as Exhibit A.

3. I have reviewed the Official Action for the application that issued on December 17, 2002.

4. In particular, I note the Examiner's objection to claims under 35 USC §112, first paragraph as not being enabling for all types of transplant. I respectfully disagree with the Examiner for the reasons that follow.

5. Experiments have been conducted by me or under my supervision which demonstrate that inhibiting Fgl2 is useful in prolonging survival of a cardiac allograft. The results of the experiments are summarized below.

6. Heterotopic cardiac transplants were performed in the groin of C57Bl/6J mice. The ascending aorta and pulmonary artery of the donor heart was anastomosed to the femoral artery and the femoral vein of the recipient mouse, respectively. Cardiac allografts were observed visually for the first 30 minutes following reperfusion and then graft survival was assessed daily by palpation. Rejection was diagnosed by cessation of ventricular contractions and confirmed by histological examination.

7. Heart transplants performed in untreated mice were rejected within 5 days. Histopathology of heart grafts showed marked cellular infiltration and expression of Fgl2 in inflammatory cells within rejecting grafts. In contrast, marked increased survival of hearts was seen in mice treated with 100 ug of an antibody to Fgl2 on days 1, 3 and 5. (See Figure 1 attached as Exhibit B.) No Fgl2 was seen within grafts and histology appeared near normal in the treated mice.

8. In view of the foregoing, I submit that the application does support a method of treating any type of transplant by inhibiting Fgl2.

9. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and, further, that these statements were made with the knowledge that wilful false

statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such a wilful false statement may jeopardize the validity of the application or any patent issuing thereon.

May 2 '03
Date

Gary Levy